JD NO	JA DKT	API NO	D	SEC(1)	SEC(2)	WELL NAME	FIELD NAME	PROD	PURCHASER
8417177	F-8A-076310	4221934087		103		MONTGOMERY ESTATE-DAVIES NCT-2 #109	LEVELLAND	17.9	AMOCO PRODUCTION
8417097	F-8A-075755	4221934083		103		MONTGOMERY ESTATE-DAVIES NCT-2 #114	LEVELLAND	15.0	AMOCO PRODUCTION
8417010	F-08-072955	4238931404		102-4		REEVES "AD" FEE #3	JESS BURNER	35.4	CONOCO INC
8417060	F-08-075109	4243131381		103		STERLING "M" FEE #4	CONGER (PENN)	0.0	VALERO TRANSMISSI
8417086	F-08-075644	4243131373		102-4		STERLING "I" FEE #8	CONGER SW	0.0	VALERO TRANSMISSI
8417101	F-8A-075837	4216532550		103		WHARTON UNIT #119	HARRIS	11.3	PHILLIPS PETROLEU
8417095	F-8A-075739	4216532665		103		WHARTON UNIT #139	HARRIS	49.3	PHILLIPS PETROLEU
8417168	F-8A-076263	4216532666		103		WHARTON UNIT #140	HARRIS	11.3	PHILLIPS PETROLEU
-TEXCOLADA OIL CO				RECEIVED:	01/20/84	JA: TX			
8417133	F-7B-076081	4213331151		102-4		A E HENSLEE #2	TIN CUP	50.0	NORTHERN GAS PROD
8417132	F-7B-076078	4213331894		102-4		BOWEN WALTON #1	TIN CUP	20.0	NORTHERN GAS PROD
8417134	F-7B-076087	4214300000		108		FRED HUFFMAN #1	DESDEMONA E	21.0	NORTHERN GAS PROD
8417131	F-7B-076075	4213331445		102-4		HENSLEE "A" #3	TIN CUP	30.0	NORTHERN GAS PROD
-THOMPSON J CLEO & JAMES CLEO JR				RECEIVED:	01/20/84	JA: TX			
8416994	F-7C-072270	4210534472		103		INGHAM "C" #1	INGHAM (DEVONIAN)	790.0	
8416968	F-7C-068733	4210500000		107-TF		UNIVERSITY 30-7W #2	UNIVERSITY 31 (STRAWN	0.0	PHILLIPS PETROLEU
-THROCKMORTON GAS SYSTEMS				RECEIVED:	01/20/84	JA: TX			
8416929	F-7B-038908	4244700000		102-4		R A BROWN "Q" #5 (05056)	VAIDA (CADDO)	0.0	WARREN PETROLEUM
-TOM BROWN INC				RECEIVED:	01/20/84	JA: TX			
8417098	F-7C-075757	4243533001		103	107-TF	HILL-MRS MAY M RAY "H" #1	ALDWELL (RANCH) CANYO	73.0	LONE STAR GAS CO
-TOM MCGEE CORP				RECEIVED:	01/20/84	JA: TX			
8417023	F-10-073637	4229531297		107-TF		DICKINSON #1	PEERY (CLEVELAND)	365.0	DIAMOND CHEMICALS
-TXO PRODUCTION CORP				RECEIVED:	01/20/84	JA: TX			
8416965	F-06-067428	4240131221		102-4		BOLTON "A" #4	MINDEN (TRAVIS PEAK 8	361.0	DELHI GAS PIPELIN
8417185	F-08-076389	4238900000		103		BURNER #1	JESS BURNER	15.0	CONOCO INC
8416973	F-10-069726	4235731274		103		DANIEL "E" #1	DANIEL	270.0	DELHI GAS PIPELIN
8416992	F-04-072154	4235500000		103		DRYDEN #1	EAST STRATTON (MIDDLE	0.0	DELHI GAS PIPELIN
8417070	F-7C-075320	4223500000		103		LINDLEY "40" #8	ROCK PEN (CANYON)	75.0	NORTHERN NATURAL
8416969	F-10-069081	4229531252		102-4		METHODIST HOME #2	D G	292.0	DELHI GAS PIPELIN
8417001	F-02-072543	4223931843		102-4		MOORE J-1	MORALES (3480)	0.0	DELHI GAS PIPELIN
8416998	F-02-072389	4223900000		102-4		POWERS G-1	MORALES (4410)	0.0	DELHI GAS PIPELIN
8417018	F-06-073348	4206730425		102-4		SIMPSON "D" #4	AVINGER (PETTIT)	0.0	DELHI GAS PIPELIN
8417178	F-10-076326	4235731444		102-4		SPICER #3	BOOKER N (MORROW UPPE	360.0	DELHI GAS PIPELIN
8416966	F-06-067698	4240131346		102-4		TEXAS UTILITIES #1	LANEVILLE NE (PETTIT	0.0	DELHI GAS PIPELIN
8416999	F-7B-072417	4241735194		102-4		WALKER-BUCKLER 79 #2	ROCKWELL (PALO PINTO)	30.0	DELHI GAS PIPELIN
8417002	F-02-072545	4223931637		102-4		WATSON B-2	MORALES (4260)	0.0	DELHI GAS PIPELIN
8416971	F-10-069644	4229531257		103		YAUCK #1	FOLLETT WEST	300.0	DELHI GAS PIPELIN
-UNION OIL COMPANY OF CALIF				RECEIVED:	01/20/84	JA: TX			
8417127	F-08-076049	4200333586		103		DOLLARHIDE UNIT #14-23-C	DOLLARHIDE (CLEAR FOR	10.0	DOLLARHIDE GASOLI
8417126	F-08-076048	4200333584		103		DOLLARHIDE UNIT #14-24-C	DOLLARHIDE (CLEAR FOR	15.0	DOLLARHIDE GASOLI
8417193	F-08-076451	4200333676		103		DOLLARHIDE UNIT #8-25-C	DOLLARHIDE (CLEAR FOR	30.0	DOLLARHIDE GASOLI
-UNITED PETROLEUM CORP				RECEIVED:	01/20/84	JA: TX			
8417135	F-10-076091	4223331699		103		CROSBY-HATCHER "B" #1	PANHANDLE-HUTCHINSON	54.0	DIAMOND CHEMICALS
-VERNON E FAULCONER INC				RECEIVED:	01/20/84	JA: TX			
8417019	F-06-073567	4240100000		108-ER		BURTON #1 GAS UNIT #039429	OAKHILL (TRAVIS PEAK)	0.0	LONE STAR GAS CO
-VORTT EXPLORATION CO INC				RECEIVED:	01/20/84	JA: TX			
8417039	F-7B-074284	4236300000		102-4		MURPHY-STONE UNIT WELL #1	MINERAL WELLS SOUTH (	0.0	SOUTHWESTERN GAS
-WARREN PETR CO A DIV OF GULF OIL CO				RECEIVED:	01/20/84	JA: TX			
8417089	F-08-075685	4210333194		103		W N WADDELL ETAL (TRA) #1285	SAND HILLS (TUBB)	193.6	EL PASO NATURAL G
8417090	F-08-075686	4210333192		103		W N WADDELL ETAL (TRA) #1287	SAND HILLS (TUBB)	28.2	EL PASO NATURAL G
-WESLEY SENKEL INC				RECEIVED:	01/20/84	JA: TX			
8417189	F-09-076437	4250336446		103		SENKEL-HAWKINS #A-1	LANGSTON-KLIENER (STR	0.0	MID-STATE GAS COR
8417190	F-09-076438	4250337218		103		SENKEL-HAWKINS #A-3	LANGSTON-KLEINER (STR	0.0	MID-STATE GAS COR
8417191	F-09-076439	4250337318		103		SENKEL-HAWKINS #A-4	LANGSTON-KLEINER (STR	0.0	MID-STATE GAS COR
-WICHITA INDUSTRIES INC				RECEIVED:	01/20/84	JA: TX			
8417116	F-7B-075945	4242932969		103		PETER SWENSON #53	STEPHENS COUNTY REGUL	36.5	WARREN PETROLEUM
8417115	F-7B-075914	4242933523		102-4		PETER SWENSON #56	SMOKEN-HAG	54.7	WARREN PETROLEUM
-WILLIAMS OIL CO				RECEIVED:	01/20/84	JA: TX			
8417149	F-08-076178	4249531615		103		MCCUTCHEN #1	KEYSTONE (COLBY)	91.0	CABOT PIPELINE CO
-WILSON ENERGY INC				RECEIVED:	01/20/84	JA: TX			
8417173	F-08-076301	4232931199		102-4		EVELYN KOONCE #1	BETTY SUE (STRAWN)	77.0	PHILLIPS PETROLEU
8417175	F-7C-076304	4210533988		103		UNIVERSITY 8 "B" 6 "G"	FARMER (SAN ANDRES)	9.0	J L DAVIS
8417174	F-7C-076303	4210533987		103		UNIVERSITY 8 "B" 8 "G"	FARMER (SAN ANDRES)	10.0	J L DAVIS
-WOLSEY OIL INC				RECEIVED:	01/20/84	JA: TX			
8417152	F-09-076206	4223700000		107-PE		J B CLAY "D" 045892	PLEMONS CONGLOMERATE	20.0	LONE STAR GAS CO
-WOOD MCSHANE & THAMS				RECEIVED:	01/20/84	JA: TX			
8417106	F-08-075897	4249531628		103		KEYSTONE CATTLE #11-C RRC #27106	KEYSTONE (COLBY)	12.3	WESTAR TRANSMISSI
-WOOLF & MAGEE INC				RECEIVED:	01/20/84	JA: TX			
8417188	F-03-076427	4237330554		102-4		JACK DILLON #1	DALLARDSVILLE (WILCOX	176.0	HOUSTON PIPELINE

[FR Doc. 84-4685 Filed 2-21-84; 8:45 am]

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federal register

Wednesday
February 22, 1984

Part V

Department of Education

34 CFR Part 690

Pell Grant Program; Cost of Attendance; Final Rule

DEPARTMENT OF EDUCATION

34 CFR Part 690

Pell Grant Program; Cost of Attendance

AGENCY: Department of Education.

ACTION: Final regulations.

SUMMARY: The Secretary is issuing final regulations governing the calculation of student's cost of attendance for the Pell Grant Program for the 1984–85 award year. These regulations are based upon Section 4 of the Student Loan Consolidation and Technical Amendments Act of 1983, Pub. L. 98–79. This regulation will affect the institution's calculation of room and board for students who do not reside at home or in institutionally owned or operated housing. This will increase the cost of attendance for these students, thus increasing their scheduled awards.

EFFECTIVE DATE: These regulations take effect 45 days after publication in the **Federal Register** or later if Congress takes certain adjournments. If you want to know the effective date of these regulations, call or write the Department of Education contact person. When these regulations become effective, they will apply to Pell Grant awards made for the 1984–85 award year (beginning July 1, 1984).

FOR FURTHER INFORMATION CONTACT: Brian Kerrigan, Chief, Pell Grant Policy Section or Gail Cornish, Pell Grant Program Specialist, Office of Student Financial Assistance, ROB–3, Room 4318, 400 Maryland Avenue, S.W., Washington, D.C. 20202, Telephone (202) 472–4300.

SUPPLEMENTARY INFORMATION: Section 4 of the Student Loan Consolidation and Technical Amendments Act of 1983, Pub. L. 98–79, provides that, with one exception, the cost of attendance criteria used for calculating Pell Grant awards for the 1983–84 award year shall be used to calculate such awards for the 1984–85 award year. The exception covers the room and board allowance for students who neither reside at home nor in institutionally owned or operated housing.

For the 1983–84 award year, the room and board allowance for these students is $1,100. However, for the 1984–85 award year, institutions which these students are attending will have some discretion in determining that allowance. Institutions are to establish a standard allowance based on the expenses reasonably incurred by these students for room and board costs which shall be at least $1,100 but not more than $1,600.

In order to fully implement this new provision, changes have been made to cover the situation where a student contracts with the institution for room or board. For the 1983–84 award year, students contracting with the institution solely for board receive a $475 room allowance. Conversely, students contracting with the institution solely for a room, receive a $625 board allowance. For the 1984–85 award year, a student contracting with the institution solely for board will receive a room allowance equal to 40 percent of the standard allowance of between $1,100 and $1,600 developed by the institution for room and board, while students contracting with the institution solely for a room will receive a board allowance equal to 60 percent of that standard allowance. These percentages maintain the proportional relationship between room and board costs in the existing regulation since the $475 room allowance in the existing regulation is approximately 40 percent of the $1,100 room and board allowance while the $625 board allowance is approximately 60 percent of that room and board allowance.

For example, if a student contracts with an institution for room, but does not contract for board, and the standard allowance determined by the institution for room and board is $1,400, the room and board for this student for the 1984–85 award year would be $840 for board expenses (i.e. 60 percent of $1,400) plus the contracted amount for room.

Finally, for a student who contracts with the institution for board for less than 7 days a week, a daily board rate will be computed for the student based on 60 percent of the standard amount established by the institution for room and board. Thus to continue the previous example, if sixty percent of the standard amount is $840 and the academic year consists of 280 days, the daily rate for board would be $3 ($840 divided by 280). This daily rate would then be multiplied by the number of days in the academic year that are not covered by the board contract, and the result would be added to the contracted amount for board. Assuming the contracted amount for board is $700 for the academic year, and the contract provides for three meals a day for 200 days, the number of days not covered by contract would be 80 (280 minus 200). Eighty multiplied by the daily rate of $3 equals $240. Thus the allowance for board in this example is $940 ($240 + $700).

To further simplify these regulations, § 690.56—"Attendance costs for students who are charged for a program whose length is less then the academic year"—has been deleted and combined with § 690.55 to read—"Attendance costs for students are charged for a program whose length is greater than or less than an academic year." The components of both of these sections were the same, therefore a consolidation simplifies the regulations.

Executive Order 12291

These regulations have been reviewed by the Department in accordance with Executive Order 12291. They are classified as non-major because they do not meet the criteria for major regulations established in the order.

Regulatory Flexibility Act Certification

The Secretary certifies that these regulations will not have a significant economic impact on a substantial number of small entities. These regulations will only affect the determination of a student's cost of attendance and the amount of the Pell Grant award a student receives. They will not have an impact on small entities as defined in the Act.

Waiver of Notice of Proposed Rulemaking

Section 4 of Pub. L. 98–79 specifies that, with one exception, the cost of attendance criteria used to calculate grants in award year 1983–84 for the Pell Grant Program shall be used for that purpose for award year 1984–85. The exception, i.e. the allowance for room and board for students who neither live at home nor in institutionally owned or operated housing, is also quite specific in the statute. Further, the proportional relationship between room and board costs is maintained in the situation where a student contracts only for a room or only for board. Therefore, since the regulations merely restate the law and establish no new substantive policy, the Secretary has determined that resort to proposed rulemaking in this instance is unnecessary within the meaning of 5 U.S.C. 553(b).

List of Subjects in 34 CFR Part 690

Administrative practice and procedure, Education, Education of disadvantaged, Grant programs—education, Student aid.

Citation of Legal Authority

A citation of statutory or other legal authority is placed in parentheses on the line following each substantive provision of these regulations.

(Catalog of Federal Domestic Assistance Number 84.063, Pell Grant Program)

Dated: February 15, 1984.

T. H. Bell,

Secretary of Education.

The Secretary amends Part 690 of Title 34 of the Code of Federal Regulations as set forth below:

1. Subpart E of the Table of Contents of Part 690 is revised to read as follows:

PART 690—PELL GRANT PROGRAM

Subpart E—Cost of Attendance

2. Subpart E of Part 690 is revised to read as follows:

Subpart E—Costs of Attendance

§ 690.51 Allowable costs of attendance—general.

(a) Except as provided in §§ 690.54–690.57, a student's cost of attendance means—

(1) The tuition and fees charged to a full-time undergraduate student for an academic year by the institution he or she is attending as determined under § 690.52;

(2) Room and board costs for an academic year as determined under § 690.53; and

(3) An allowance of $400 for books, supplies, and miscellaneous expenses for an academic year.

(b) An institution must be able to justify and document the cost of attendance figures established under this subpart.

(Sec. 4 of Public Law 98–79)

§ 690.52 Tuition and Fees.

(a)(1) An institution shall determine the tuition and fees charged a full-time undergraduate student by calculating either—

(i) The actual amount it charges each full-time undergraduate student for tuition and fees for an academic year, or

(ii) The average amount it charges full-time undergraduate students for tuition and fees for an academic year.

(2) However, the institution must use the option it selects under paragraph (a)(1) of this section to determine the tuition and fee charges of all its students under this part.

(b) If an institution establishes its tuition and fee charges on a residency requirement basis (e.g. In-State and Out-of-State) and elects to calculate an average tuition and fee charge, it shall establish a separate average charge for each different residency based classification.

(c) An institution may determine a separate average charge for any other distinct classification upon which it bases tuition and fee charges.

(Sec. 4 of Public Law 98–79)

§ 690.53 Room and board.

The institution shall determine a student's room and board costs for an academic year as follows—

(a) For a student who enters into a contract with the institution for room and/or board, the institution shall choose one of the following cost options but must use the option it selects for all students. The two options are:

(1) The actual amount it charges each student for:

(i) Room and board for an academic year,

(ii) Room only, plus an allowance equal to 60 percent of the standard allowance established by the institution in paragraph (b)(2) of this section, for board for an academic year, or

(iii) Board only, plus an allowance equal to 40 percent of the standard allowance established by the institution in paragraph (b)(2) of this section, for room for an academic year, or

(2) The average amount it charges most students for:

(i) Room and board for an academic year,

(ii) Room only, plus an allowance equal to 60 percent of the standard allowance established by the institution in paragraph (b)(2) of this section, for board for an academic year, or

(iii) Board only, plus an allowance equal to 40 percent of the standard allowance established by the institution in paragraph (b)(2) of this section, for room for an academic year.

(b) For a student who does not enter into a contract with the institution for either room or board, the student shall receive—

(1) An allowance of $1,100 for an academic year if he or she lives in the home of his or her parents, or

(2) An allowance of at least $1,100 but not more than $1,600 for an academic year if he or she does not live in the home of his or her parents. This amount shall be a standard amount determined by the institution based upon the expenses reasonably incurred by such students, and shall apply to all students covered under this subparagraph.

(c) If a student enters into a contract with the institution for board for less than 7 days a week, a daily rate will be computed based upon an allowance of 60 percent of the standard amount established by the institution in paragraph (b)(2) of this section and used for those days of the academic year not covered by the contract. This amount will be added to the cost established under paragraph (a)(1) or (a)(2) of this section.

(Sec. 4 of Public Law 98–79)

§ 690.54 Attendance costs for students in correspondence study programs.

The cost of attendance for a student enrolled in a correspondence study program means—

(a) Actual tuition and fees charged to the student for an academic year; and

(b) If incurred in fulfilling a required period of residential training, room and board costs based on—

(1) The actual amount charged to the student by the institution; or

(2) The standard allowance established in § 690.53(b) prorated in the same ratio as the course work completed in residential training bears to the course work for the academic year.

(Sec. 4 of Public Law 98–79)

§ 690.55 Attendance costs for students who are charged for a program whose length is greater than or less than an academic year.

The cost of attendance for a student who is charged tuition and fees for a program whose length is greater than or less than the length of the academic year at the institution, is determined by adding—

(a)

$$\text{Tuition and fees} \times \frac{\text{clock or credit hours in the academic year}}{\text{clock or credit hours in the program}}$$

and

(b) Room and board costs as determined under § 690.53; and

(c) An allowance of $400 for books, supplies and miscellaneous expenses.

(Sec. 4 of Public Law 98–79)

§ 69.56 Attendance costs for incarcerated students.

(a) The cost of attendance for a student who is incarcerated for whom at least one-half of his or her room and board expenses is provided includes—

(1) Tuition and fees as determined under § 690.52; and

(2) An allowance of $150 for books and supplies.

(b) The cost of attendance for a student who is incarcerated and for whom less than one-half of his or her room and board expenses is provided is the same as that allowed for a student who is not incarcerated.

(Sec. 4 of Public Law 98–79)

§ 690.57 Attendance costs for students at U.S. Armed Forces Academies.

A student enrolled at the U.S. Military Academy at West Point, the U.S. Naval Academy, the U.S. Air Force Academy or the U.S. Coast Guard Academy is considered to have no cost of attendance.

(Sec. 4 of Public Law 98–79)

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Wednesday
February 22, 1984

Part VI

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 172
Food Additives Permitted for Direct Addition to Food for Human Consumption; Aspartame; Denial of Requests for Hearing; Final Rule

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 172

[Docket Nos. 75F-0355 and 82F-0305]

Food Additives Permitted for Direct Addition to Food for Human Consumption; Aspartame

AGENCY: Food and Drug Administration.

ACTION: Denial of requests for hearing; final rule-related.

SUMMARY: The Food and Drug Administration (FDA) is denying the requests for a hearing on certain safety issues related to the amendment to the food additive regulation concerning aspartame that provides for the safe use of the substance in carbonated beverages and carbonated beverage syrup bases. After reviewing the objections to the amendment and the requests for a hearing, FDA has concluded that the objections do not raise issues of material fact that justify granting a hearing on a food additive regulation.

FOR FURTHER INFORMATION CONTACT: Anthony P. Brunetti, Bureau of Foods (HFF-334), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-427-5690.

SUPPLEMENTARY INFORMATION:

I. Introduction

Aspartame (*N*-*L*-α-aspartyl-*L*-phenylalanine 1-methyl ester) is the nutritive methyl ester of a dipeptide formed from phenylalanine and aspartic acid. G. D. Searle & Co., 4901 Searle Parkway, Skokie, IL 60077, originally petitioned in 1973 for approval of its use as a sweetener and flavor enhancer in dry foods. FDA approved the petition in a final regulation published in the **Federal Register** of July 26, 1974 (39 FR 27317), and codified at 21 CFR 172.804.

FDA received formal objections to this regulation and requests for a hearing to investigate certain alleged toxic effects of aspartame. FDA granted the request for a hearing and established a Public Board of Inquiry (the Board), nominated from scientists outside the agency, to hear expert testimony and evaluate the scientific issues raised in the objections. Subsequently, FDA stayed the regulation (40 FR 56907; December 5, 1975) and delayed the Board's convening while an extensive audit of the authenticity of certain toxicological studies on aspartame was conducted. Of the 15 pivotal studies, 3 were reviewed by an FDA task force and 12 by scientists from Universities Associated for Research and Education in Pathology, Inc. (UAREP), a consortium of 9 universities. Following the finding by UAREP that the animal studies were authentic, the Board convened a public hearing; it completed the hearing and issued its report in 1980 (Aspartame, Decision of the Public Board of Inquiry, Docket No. 75F-0355) (Board's decision).

In the **Federal Register** of July 24, 1981 (46 FR 38285), the Commissioner of Food and Drugs reviewed the Board's conclusions and announced his final decision that aspartame was safe within the meaning of section 409(c) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)). The Commissioner specifically determined that, on the basis of available data, aspartame consumption would not cause brain damage such as mental retardation, brain lesions, or endocrine dysfunction, nor would it cause brain tumors. FDA then reinstated the original regulation (46 FR 50947; October 16, 1981), approving aspartame for the following uses as a sweetener: dry sugar substitutes in free-flowing and tablet form; cold cereals; chewing gum; and dry bases for beverages, instant coffees and teas, puddings and gelatins, and dairy analog toppings (21 CFR 172.804(c)). None of the parties who originally requested a hearing on the regulation objected to or sought judicial review of the agency's final decision to reinstate the regulation approving the dry uses of aspartame.

II. Aspartame For Use In Carbonated Beverages

A. Regulation Approving Use

In the **Federal Register** of July 8, 1983 (48 FR 31376), FDA issued a final rule that amended § 172.804 by adding new paragraph (c)(6) to permit the additional use of aspartame as a sweetener in carbonated beverages and carbonated beverage syrup bases. That regulation responded to a petition filed by G. D. Searle & Co. (47 FR 46140; October 15, 1982). Before approving this new use, the agency reviewed, among other safety issues, the potential neurotoxicity of the components and decomposition products of aspartame, the stability of aspartame in carbonated beverages, and the potential impact on health of increased consumption of aspartame resulting from its additional use in carbonated beverages.

In the preamble to the final rule, FDA also considered and responded to a number of safety issues raised in comments on the carbonated beverage petition (48 FR 31376 at 31378-31381). These comments expressed particular concern about potential adverse effects of aspartame's component amino acids on the brain, and the potential for exposure to toxic levels of decomposition products, including methanol, from aspartame's use in carbonated beverages. FDA based its approval of aspartame for use in carbonated beverages on its evaluation of clinical studies which were submitted by the petitioner to supplement animal study data supplied with the dry uses petition, data from other relevant studies in the scientific literature, and data contained in comments submitted on the petition (*id.*). These data are all included in the administrative record of Docket No. 82F-0305.

B. Objections and Requests for a Hearing and a Stay

Two objections were filed to the July 8, 1983 regulation approving the use of aspartame in carbonated beverages. The objections contended that numerous safety issues had not been adequately considered by the agency before the promulgation of the regulation, and requested that the regulation be stayed pending examination of those issues in a public hearing. The two parties objecting to the regulation on the basis of unresolved safety issues were James S. Turner, 1424 16th St. NW., Washington, DC 20036, objecting on behalf of himself and the Community Nutrition Institute, 1146 19th St. NW., Washington, DC 20036; and Woodrow C. Monte, Director, Food Science and Nutritional Laboratories, Arizona State University, Tempe, AZ. In addition, Richard J. Wurtman, Massachusetts Institute of Technology, Cambridge, MA, commented on the regulation, but did not request a hearing or a stay of the regulation. Before publication of the final rule approving the use of aspartame in carbonated beverages, Dr. Wurtman wrote a series of letters to FDA in which he expressed his concern about potential adverse effects on brain function of ingesting high levels of carbohydrate and aspartame, and reported the results of some experiments conducted in his laboratory.

FDA denied the requests to stay the effectiveness of the carbonated beverage regulation (48 FR 52899; November 23, 1983), because the public interest did not require it. FDA briefly evaluated each contention of the objections, and concluded that they failed to create doubts about the safety of aspartame significant enough to stay the regulation approving the use of aspartame in carbonated beverages. In that document, FDA also confirmed July 8, 1983, as the effective date of the

regulation authorizing the use of aspartame in carbonated beverages.

C. Standard for Granting a Hearing and Character of the Objections

Section 409(f) of the act provides that any person adversely affected by a final food additive regulation may file objections, specifying with particularity the provisions of the order "deemed objectionable, stating reasonable grounds therefor," and request a public hearing based upon such objections. However, the Commissioner may deny the hearing request if the objections to the regulation do not raise genuine and significant issues of fact that can be resolved at a hearing. Specific criteria for determining whether a request for a hearing has been justified are codified at 21 CFR 12.24(b). The pertinent criteria in 21 CFR 12.24(b) for granting a hearing are:

(1) There is a genuine and substantial issue of fact for resolution at a hearing. A hearing will not be granted on issues of policy or law.

(2) The factual issues can be resolved by available and specifically identified reliable evidence. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions.

(3) The data and information submitted, if established at a hearing, would be adequate to justify resolution of the factual issue in the way sought by the person. A hearing will be denied if the Commissioner concludes that the data and information submitted are insufficient to justify the factual determination urged, even if accurate.

(4) Resolution of the factual issue in the way sought by the person is adequate to justify the action requested. A hearing will not be granted on factual issues that are not determinative with respect to the action requested, e.g., if the Commissioner concludes that the action would be the same even if the factual issue were resolved in the way sought * * *.

A party seeking a hearing is required to meet a "threshold burden of tendering evidence suggesting the need for a hearing." *Costle* v. *Pacific Legal Foundation*, 445 U.S. 198, 214–215 (1980) *reh. den.* 446 U.S. 947 (1980), citing *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 620–621 (1973). An allegation that a hearing is necessary to "sharpen the issues" or "fully develop the facts" does not meet this test. *Georgia Pacific Corp.* v. *U.S. E.P.A.*, 671 F.2d 1235, 1241 (9th Cir. 1982). If a hearing request fails to identify any evidence that would be the subject of a hearing, there is no point in holding one. In judicial proceedings, courts are authorized to issue summary judgment without an evidentiary hearing whenever they find that there are no material issues of fact in dispute and a party is entitled to judgment as a matter of law. See Rule 56, Federal Rules of Civil Procedure. The same principle applies in administrative proceedings.

A hearing request must not only contain evidence, but that evidence should raise a material issue of fact concerning which a meaningful hearing might be held. *Pineapple Growers Association* v. *FDA*, 673, F.2d 1083, 1085 (9th Cir. 1982) (where the issues raised in the objection are, even if true, legally insufficient to alter the decision, the agency need not grant a hearing). *Dyestuffs and Chemicals, Inc.* v. *Flemming*, 271 F.2d 281 (8th Cir. 1959) *cert. denied*, 362 U.S. 911 (1960). FDA need not grant a hearing in each case where an objection submits additional information or posits a novel interpretation of existing information. See *United States* v. *Consolidated Mines & Smelting Co.*, 455 F.2d 432 (9th Cir. 1971). Stated another way, a hearing is justified only if the objections are made in good faith and if they "draw in question in a material way the underpinnings of the regulation at issue." *Pactra Industries* v. *CSPC*, 555 F.2d 677 (9th Cir. 1977). Finally, courts have uniformly recognized that a hearing need not be held to resolve questions of law or policy. See *Citizens for Allegan County, Inc.* v. *FPC*, 414 F.2d 1125 (D.C. Cir. 1969); *Sun Oil Co.*, v. *FPC*, 256 F.2d 233, 240 (5th Cir.), *cert. denied*, 358 U.S. 872 (1958).

Even if the objections raise material issues of fact, FDA need not grant a hearing if those same issues were adequately raised and considered in the earlier aspartame proceeding leading to the approval of aspartame for dry uses. Once an issue has been so raised and considered, a party is estopped from raising that same issue in a later proceeding without new evidence. It is illogical not to recognize that the various judicial doctrines dealing with finality can be validly applied to the administrative process. In explaining why these principles "self-evidently" ought to apply to an agency proceeding, the D.C. Circuit wrote:

The underlying concept is as simple as this: Justice requires that a party have a fair chance to present his position. But overall interests of administration do not require or generally contemplate that he will be given more than a fair opportunity.

Retail Clerks Union, Local 1401, R.C.I.A., v. *NLRB*, 463 F.2d 316, 322 (D.C. Cir. 1972). See *Costle* v. *Pacific Legal Foundation, supra* at 1106. See also *Pacific Seafarers, Inc.* v. *Pacific for East Line, Inc.*, 404 F.2d 804 (D.C. Cir. 1968).

In sum, a hearing request should present sufficient credible evidence to raise a material issue of fact which has not already been the subject of an administrative hearing. As is detailed in section III below, the hearing requests of Mr. Turner and Dr. Monte either do not present sufficient credible evidence to warrant a hearing or, where credible evidence is presented, even if true, that evidence does not raise a material issue of fact. Moreover, the hearing request of Mr. Turner, who was a participant in the hearing on the dry uses of aspartame, raises substantially the same objections that he had presented in the administrative hearing on the dry uses of aspartame. Those issues were considered by the Board's decision at p. 2 and reviewed in the Commissioner's decision (46 FR 38285), and Mr. Turner did not seek judicial review or administrative reconsideration of the agency's final approval for the dry uses of aspartame. Mr. Turner has thus had a fair opportunity to present his position on these issues and an additional hearing on the same issues is unwarranted.

III. Analysis of the Objections

A. Introduction

This section examines the specific issues identified in the objections to the regulations approving the use of aspartame in carbonated beverages. This document deals with each issue, but certain of the issues are considered at greater length because they have not been covered as extensively in public documents. Similar issues have been combined for ease of discussion and analysis. The general categories are: brain damage, decomposition products, consumption levels, cancer, interpretation of data from clinical studies, quality of data, and labeling. In responding to the various issues raised by the objections, the agency incorporates by reference all materials in the administrative record (Docket Nos. 75F–0355 and 82F–0305).

B. Brain Damage

1. *Brain lesions and mental retardation.* Mr. Turner's objection has expressed concern about aspartame's potential for causing mental retardation, brain lesions, and other adverse behavorial and physiological effects, because of adverse responses to its component amino acids, phenylalanine and aspartate. The issue was raised by Mr. Turner (p. 2) at the hearing on the dry uses of aspartame and was fully

considered by the Board and the Commissioner. Thus, further hearing on this issue is unwarranted. The following discussion summarizes the agency's consideration of this brain damage issue and explains the basis for the agency's conclusion that aspartame has been shown to be safe.

Because the phenylalanine and aspartate constituents of aspartame are also constituents of normal dietary protein, any risk from aspartame ingestion would occur because of the exposure to these amino acids in excess of normal exposure from dietary sources.

Very high doses of aspartate given by gavage or injection have been associated with discrete lesions in the brains of rodents. However, when the same high levels of aspartate or aspartame are administered in the diet to rodents, plasma levels of aspartate do not reach the concentrations required to produce lesions in rodent brains (46 FR 38285 at 38287). Continuous, extremely high plasma levels of phenylalanine, the other constituent amino acid of aspartame, have been known to produce mental retardation in the fetus of phenylketonuric mothers and in infants with phenylketonuria (PKU). However, an adequate margin of safety exists between the levels of phenylalanine known to produce mental retardation and those resulting even from exaggerated exposure to aspartame in carbonated beverages.

The possibility of brain lesions and mental retardation resulting from the use of aspartame was one of the major issues raised by Mr. Turner in his objection to the regulation approving the dry uses of aspartame and was fully considered at the hearing. The Board concluded that the ingestion of aspartame at levels that would be higher than those expected from consumption of aspartame for dry uses and in carbonated beverages could not be expected to increase the incidence of mental retardation, brain damage, or dysfunction of neuroendocrine regulatory system (Board's decision at p. 39). Subsequently, the Commissioner again reviewed the available evidence regarding brain lesions in rodents associated with asparatate and mental retardation related to phenylalanine. The Commissioner concluded that an adequate margin of safety exists between the amino acid levels resulting even from exaggerated exposure to aspartame and those observed to produce brain lesions in the rodent and mental retardation in PKU-related conditions (46 FR 38285 at 38288).

This issue has already been thoroughly considered in the earlier proceeding leading to the approval of aspartame for dry uses and Mr. Turner was given a full and fair opportunity to present his views in the earlier proceeding. Moreover, Mr. Turner could have sought judicial review or administrative reconsideration of the Commissioner's decision on this point, but did not challenge it. Accordingly, he is now estopped from raising the issue without new evidence unavailable at the time of the earlier proceeding. His objection presents no new information on this issue. A hearing is not justified if no data and information are submitted to support the factual determination urged (21 CFR 12.24(b)(3)).

2. *Potential adverse behavioral effects.* The amino acids, phenylalanine, tyrosine (a metabolite of phenylalanine), and tryptophan serve as precursors in the biosynthesis of neurotransmitters in both the periphery and the brain. According to the objections (Turner, p. 4; Monte, p. 5), the data submitted by Dr. Wurtman require the agency to hold a hearing to determine whether aspartame ingestion may alter the brain levels of these precursor amino acids and, in turn, neurotransmitter function, thereby leading to potentially adverse behavioral effects.

Although theories have been postulated to correlate changes in neurotransmitter function with cognitive or affective behavior, the state-of-the-art is such that little definitive evidence is available to support such relationships.

The data submitted by Dr. Wurtman (Ref. 1) in his comments on the carbonated beverage petition demonstrate increases in the plasma amino acid concentrations of phenylalanine and tyrosine in the human and rat following administration of large doses of aspartame to fasted subjects. The same data also demonstrate increases in the concentration of phenylalanine and tyrosine in the brain of the rat. Dr. Wurtman asserts that these increases in brain tyrosine and phenylalanine might result in changes in catecholamine neurotransmitters synthesized from these precursor amino acids. Drs. Wurtman (Ref. 2) and LaChance (Ref. 3) submitted comments that also postulated that these potential changes in neurotransmitters might lead to unpredictable behavioral effects, but submitted no evidence that would demonstrate that such behavioral effects have been observed or that they might plausibly be anticipated other than on the basis of the theories presented.

In the final regulation approving the use of aspartame for use in carbonated beverages, FDA discussed the data submitted by Drs. Wurtman and LaChance and the related literature on neurochemistry and behavior, and concluded that exposure to aspartame in foods would not result in adverse behavioral effects (48 FR 31376 at 31379-31380). After FDA had approved the use of aspartame in carbonated beverages, Dr. Wurtman submitted additional data in which he measured the levels of rat brain serotonin (5-HT) and its metabolite, 5-hydroxy-indoleacetic acid (5-HIAA) (Ref. 1). An increase in 5-HT and 5-HIAA occurring after high levels of glucose intake in fasted rats was blocked by concurrent administration of a high dose of aspartame. Dr. Wurtman suggested that this inhibition or "blockage" of glucose-mediated increases in brain levels of 5-HT and 5-HIAA by very high doses of aspartame, which he observed in animal studies, might mean that consumption of aspartame by humans could interfere with their normal pattern of carbohydrate consumption. Dr. Wurtman did not provide any evidence that the observed changes in brain 5-HT and 5-HIAA levels produced a change in the eating habits, preferences, or any other behavior of the animals tested.

FDA has reviewed the data dealing with the effect of aspartame in glucose-mediated changes in brain neurotransmitters that were submitted and has concluded that they are consistent with expected results following simultaneous administration of any food containing protein with glucose. The findings represent normal physiological variations in brain neurochemicals, which are a response to a specific dietary regimen, and thus would not be expected to be associated with adverse behavioral effects.

Drs. Wurtman and Lachance have developed interesting, but untested, hypotheses. The hypotheses do not, even if true, suggest that aspartame is not safe; they suggest merely that certain chemical changes may occur as the result of ingesting aspartame. For this reason, no purpose would be served by holding a hearing, because no issue of material fact is raised by the hypotheses. Moreover, even if the hypotheses raised an issue of material fact, a hypothesis, standing alone, does not justify a hearing in the absence of data on which to base a resolution of the issue raised. No such data are identified in Dr. Wurtman's submission or in the objections. FDA, therefore, denies the request for a hearing on these issues.

C. Decomposition and Reaction Products

There is a customary battery of toxicological tests in various animal

species that is required to demonstrate the safety of a direct food additive. These tests generally are familiar to sponsors of food additive petitions. To disseminate information about these tests further, the agency has developed and published a set of publicly available guidelines describing these tests "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food" ("REDBOOK" (Ref. 4)). The "REDBOOK" also sets forth certain tests beyond the customary battery of tests that the agency requires if the chemical structure of the additive or some other factor suggests particular reasons for concern.

In support of its petition for the use of aspartame for dry uses, Searle performed a complete series of traditional toxicological studies involving laboratory animals to verify the safety of aspartame during chronic exposure (Ref. 5). The design of the studies meets or exceeds that stated in the "REDBOOK" guidelines. In addition, because a consumer could be exposed to significant quantities of aspartame on a daily basis, and occasionally to high levels of aspartame, the petitioner conducted clinical studies (studies in humans) that provided ample evidence of the safety of aspartame under predicted levels of chronic ingestion or unusual situations of high, acute exposure (Refs. 6 and 7).

Before FDA approved aspartame, Searle submitted, and FDA evaluated, more than the usual tests with respect to the decomposition of this food additive. Because it is not feasible to require manufacturers to test every decomposition product, the agency routinely does not require testing of all of them unless a particular decomposition product poses a safety question, or little is known about its toxicological profile.

With respect to the toxicity of diketopiperazine (DKP), a primary decomposition product of aspartame, Searle submitted data in support of its petition for aspartame's dry uses to establish DKP's safety (Ref. 8). The agency also anticipated that a safety problem might arise in the use of aspartame in carbonated beverages if DKP, in solution, formed nitrosamines. Accordingly, Searle submitted, and FDA evaluated, studies on the likelihood of nitrosamine formation from the use of aspartame in carbonated beverages (Ref. 9).

FDA was aware of significant scientific literature on the toxicity of the following components of aspartame: phenylalanine, aspartic acid, and methanol. The agency reviewed the safety data submitted by Searle in support of its petition for dry uses derived from animal and clinical studies and consumption studies, as well as the existing body of scientific data, and concluded that the studies demonstrated the safety of these components. The Board's decision at p. 20 and p. 38 and the Commissioner both concluded that these components are safe (46 FR 38285 at 38287).

The objections now contend that FDA has failed to dispose of the possibility that decomposition and reaction products created by the addition of aspartame to carbonated beverages and carbonated beverages syrup bases may make those products unsafe (Turner, II, p. 9).

1. *Unidentified and unsafe decomposition and reaction products.* The objections present no evidence to support their contention that unidentified decomposition products or reaction products of aspartame may be harmful (Turner, p. 9; Monte, p. 8). One objection refers to an abstract of a scientific talk which discusses the reactivity of aspartame with certain flavor components of food (aldehydes and ketones) (Monte, p. 9). Reactions between food components occur too commonly to warrant specific testing for each individual class of reaction or decomposition products. Food itself undergoes a number of reactions, for example, in cooking. As the agency pointed out in the final regulation approving the use of aspartame in carbonated beverages, the similarity of the basic dipeptide structure of aspartame to normal dietary protein provides an added measure of assurance of its safety in regard to reactivity with food components and its metabolic fate (48 FR 31376 at 31382). Because the objection has presented no data to support its concern, and because the agency has no independent basis for concern, there is no basis upon which to grant a hearing. The agency will not grant a hearing on the basis of mere unsubstantiated allegations. Further, in the absence of any data, the simple charge that there may be a safety issue regarding decomposition products calls into question the agency's policy regarding the threshold for requiring scientific testing of such products. This question is one of both policy and law, i.e., the proper legal interpretation of the safety standards of the act, and thus is not a proper issue for an evidentiary hearing.

2. *Inability to account for up to 30 percent of the sweetener.* The objection states that Searle is unable to account for as much as 30 percent of the sweetener, despite having analyzed for components expected in the usual breakdown pathways, and that a more complete breakdown occurs at temperatures above 30° C (86° F) (Turner, p. 10). As detailed in the preamble to the carbonated beverage rule, the petition for this use of aspartame included the results of extensive stability studies on carbonated beverages (48 FR 31376 at 31377). These experiments were performed with beverages stored at various temperatures for periods of up to 52 weeks. Four beverage flavors were analyzed for aspartame and five decomposition products at various intervals. Essentially all of the analyses of beverages stored at 30° C for up to 40 weeks accounted for 90 to 100 percent of the original added aspartame. The contention that 30 percent of the decomposition products are unknown is misleading, because it focuses on the results at high temperatures (40° C (104° F); 55° C (131° F)) in which the results of the analysis are not as complete as those at lower temperatures. The more complete breakdown at higher temperatures is not unexpected, and, more important, is not crucial to the determination of the safety of the breakdown products. The sum of the decomposition studies submitted with the aspartame food additive petition for use in carbonated beverages provided the necessary identification of the decomposition products and evidence of their safety. The objections present no evidence in support of the implied increase in risk from greater decomposition at the higher temperature, other than the contention that the decomposition products are "unidentified" and that higher levels of free methanol would be present. After evaluating the studies and the general body of literature on the subject, FDA concluded that there was no reason to believe that the additional decomposition products would be substantially different from those formed at lower temperatures (48 FR 31376 at 31377). The objection does not justify a hearing because it presents no evidence that calls into question the safety of these decomposition products. As discussed above in section III.C.1., the allegation that all decomposition products should be presumed to be unsafe and therefore tested raises a legal and policy issue and is not appropriate for resolution at a hearing. (The toxicity of the decomposition product methanol is discussed below.)

3. *Methanol ingestion from decomposed aspartame.* Both objections argued that aspartame's decomposition can result in exposure to adverse levels

of methanol, "a known poison," (Monte, p. 2) and that the metabolism of methanol in the body yields formaldehyde, "a known carcinogen" (Turner, p. 12) (see section III.E. below). The agency evaluated the safety issues related to the ingestion of methanol derived from aspartame in its evaluation of aspartame for dry uses and concluded that the levels of methanol resulting from the use of aspartame in carbonated beverages did not pose any safety issues because they were well below levels of exposure expected to produce toxicity (Ref. 10).

Dr. Monte's objection argued (1) that "free" methanol produced by the decomposition of aspartame in carbonated beverages is more toxic than "dietary" methanol formed by the metabolism of aspartame in the gastrointestinal tract because of the differences in metabolism and a more complete amount of absorption of "free" rather than "dietary" methanol; and (2) that the amount of "free" methanol absorbed as a result of aspartame consumption is of sufficient quantity to produce a "significant and rapid rise in methyl alcohol and formate levels in the plasma" (Monte, p. 4). The objections allege that these levels are of toxicological concern under acute or chronic use conditions, but they neither submitted nor referred to available data in support of that allegation.

a. *Free Methanol Is Not More Toxic Than Methanol Produced by the Metabolism of Aspartame in the Gastrointestinal Tract.* The objection proffered a hypothesis that the decomposition of aspartame to methanol or to any of its secondary metabolities prior to consumption poses additional safety questions regarding the continued use of aspartame in carbonated beverages, but provided no evidence to support that position (Monte, p. 3). FDA analyzed the methanol safety issue before the agency approved aspartame for dry uses and again in its evaluation of the petition for use in carbonated beverages (Ref. 10). The objection has presented no evidence of any kind to alter FDA's original evaluation. FDA cannot accept as a basis for conducting a hearing unsubstantiated hypotheses concerning issues the agency already satisfactorily resolved.

Metabolic studies performed in monkeys and submitted by Searle in support of its petition for aspartame for dry uses demonstrate that the overall metabolic disposition of the methanol moiety from aspartame is similar to that of methanol administered alone to monkeys (Ref 11). The methyl moiety appears to be rapidly and completely cleaved from aspartame in the gastrointestinal tract, and this methyl group is oxidized in essentially the same manner as "free" methanol. The only detectable difference in the pharmacokinetic properties between "free" methanol and "dietary" methanol derived from the hydrolysis of aspartame is a faster rate of absorption of the "free" methanol within the first hour. "Free" methanol is readily absorbed from the stomach whereas aspartame must pass into the small intestine before hydrolysis and absorption of the methanol can occur. This small difference in the rate of methanol absorption is not significant because the metabolism of methanol is slow and because the overall amount of methanol ultimately absorbed as a result of consumption of a given quantity of aspartame-sweetened beverage is the same.

Thus, there is no scientific basis for differentiating the "free" from the "dietary" methanol in analyzing the toxicological profile of aspartame. The agency evaluated the metabolism data early in its evaluation of the data in support of the dry use petition, and assumed that methanol was completely hydrolyzed from aspartame in the gastrointestinal tract (Ref. 11). Exposure to methanol from aspartame can be calculated on a one-to-one molar basis independent of the decomposition rate in carbonated beverages, which can vary with storage conditions. Therefore, an estimate of methanol exposure following ingestion of aspartame is provided by taking 10 percent of the weight of the aspartame dose. The objection submits no data that supports its position or discredit the agency's conclusions based on the earlier studies performed by Searle. Thus, there is no basis for granting the hearing request.

b. *The Amount of Free Methanol Absorbed from Aspartame Does Not Produce a Significant and Rapid Rise in Plasma Methyl Alcohol and Formate Levels.* One objection (Turner, p. 11) contended that FDA had incorrectly concluded that the level of dietary exposure to methanol is not of "prime importance" in assessing the safety of aspartame (48 FR 31376 at 31380). The objection did not, however, present evidence showing at what concentration methanol is toxic or that the consumption of aspartame would result in the consumption of toxic levels of methanol.

The agency does not believe that methanol exposure equivalent to 10 percent of the aspartame dose is of sufficient quantity to be of toxicological concern under acute or chronic use conditions. A study (Ref. 12) submitted by Searle in support of its petition for the dry uses of aspartame showed no detectable levels of methanol in the blood of human subjects following the ingestion of aspartame at 34 milligrams per kilogram (mg/kg) body weight (the 99th percentile level of projected ingestion across all age groups). Assuming complete hydrolysis after ingestion, this 34 mg/kg dose of aspartame is equivalent to a dose of 3.4 mg/kg body weight of methanol. The agency reviewed this study and others dealing with methanol toxicity prior to approving aspartame for dry uses and cited the data in the preamble to the final regulation approving the use of aspartame in carbonated beverages (48 FR 31376 at 31380).

Even following administration of an abuse dose of aspartame of 200 mg/kg body weight (equivalent to 20 mg/kg body weight of methanol or drinking more than 13 quarts of aspartame-sweetened orange soda) in a clinical study conducted by Searle, the mean peak blood methanol concentration reached only 26 mg per liter. The hearing request contains no evidence to suggest that even this level of methanol, consumed in free form, is toxic. Thus even if all aspartame in soft drinks decomposed prior to their consumption, the agency has no reason to believe any danger of methanol poisoning would exist. FDA remains convinced that the studies submitted by Searle in support of the dry use, and reviewed by FDA prior to the dry uses approval and again in its evaluation of the carbonated beverage petition, adequately support the agency's conclusion that there was "no cause for concern from the levels of dietary methanol resulting from the highest projected levels of aspartame consumption" (48 FR 31376 at 31381).

The agency has recently become aware, however, of clinical data that further buttress the agency's determination. Although FDA did not rely on these studies in approving the carbonated beverage petition, nor is it necessary to rely on the studies here, the agency believes that they present pertinent information that is consistent with that contained in the Searle data. This document discusses them to some extent. FDA has placed copies of the reports in the administrative record for Docket No. 82F-0305. Among these studies are some that indicate that the toxic effects of methanol are due to formate accumulation and not to formaldehyde or methanol itself (Refs. 13, 14, and 15). Formate is the oxidation product of formaldehyde which is itself formed from the metabolism of

methanol. In the Searle clinical study using abuse doses of aspartame equivalent to 20 mg/kg body weight of methanol, no significant increases were observed in plasma concentrations of formate, suggesting that the rate of formate production does not exceed its rate of urinary excretion. In fact, studies in human subjects given oral dosages of methanol of 71 to 84 mg/kg body weight showed no toxic effects with blood levels of methanol reaching 47 to 76 mg per liter 2 to 3 hours afterwards (Ref. 16). From estimates based on blood levels in methanol poisonings, it appears that the ingestion of methanol on the order of 200 to 500 mg/kg body weight is required to produce a significant accumulation of formate in the blood which may produce visual and central nervous system toxicity (Refs. 17 and 18).

The toxic doses of methanol (200 to 500 mg/kg body weight) are approximately one hundred times that ingested when aspartame is consumed at the 99th percentile level of projected chronic ingestion (10 percent of 34 mg/kg body weight aspartame, or 3.4 mg/kg body weight methanol). Moreover, orange soda, which may contain the highest concentration of aspartame in carbonated beverages (335 mg aspartame per 12 fluid ounces or 930 mg per liter), results in a lower methanol level (93 mg per liter) than that found in the average fruit juice (140 mg per liter) (Ref. 19). Under the most conservative assumption, the complete hydrolysis of aspartame to methanol, an adequate margin of safety exists for the use of aspartame in carbonated beverages. The consumption of aspartame would not result in toxicologically significant methanol and formate levels.

Finally, it is well known that much food contains significant quantities of methanol. In fruit juices, the average content of methanol is 140 mg per liter and grain alcohols (such as gin and whiskey) contain as much as 1,000 mg per liter (Ref. 19). Moreover, fresh fruits and vegetables also contain compounds that are metabolized in the body to methanol (Refs. 20 and 21). Normal metabolic processes such as purine and pyrimidine biosynthesis and amino acid metabolism require methyl groups from compounds like methanol (Ref. 22). It also appears that either methanol or formaldehyde may serve as precursors for the methyl groups in choline synthesis (Ref. 23).

The agency has concluded that, because the objection has failed to present evidence establishing at what level methanol is toxic and whether consumption of carbonated beverages containing aspartame would exceed that level, no hearing is required to reevaluate the significance of exposure to methanol from aspartame consumption. The objection submitted no data and the agency is aware of none in support of the objection's position. FDA will not grant a hearing on the basis of a mere allegation.

4. *Nitrosamines formation from DKP and toxicity of DKP.* The objections allege that the agency has "mischaracterized" and "failed to consider" data dealing with potential toxicity from DKP (Turner, p. 10) and has failed to assess the "potential danger" of nitrosamine formation by intestinal bacteria after prolonged exposure to DKP (Monte, p. 7).

a. *Nitrosation of DKP.* FDA reviewed studies conducted by Searle aimed at evaluating the nitrosation potential of aspartame and DKP before the original approval of aspartame in 1974. These studies attempted to form, under ideal conditions, the nitrosamines of aspartame and DKP and demonstrated that stable nitrosamine derivatives were difficult to form at a level detectable with the then current analytical methodology (Ref. 24). The study also demonstrated that nitrosamine derivatives of aspartame or DKP intermediates, formed under ideal laboratory conditions, were extremely unstable under physiological or aqueous conditions. Given these results, FDA concluded that it was most unlikely that any nitrosamines could remain in the gastrointestinal tract or in an aqueous solution, such as soft drinks, containing aspartame or DKP (Ref. 25).

The objections further contend that the agency has been remiss in not reexamining the nitrosamine issue, employing more sensitive, modern analytical methodology. In support of this contention, one objection (Monte, p. 7) cites a recent publication describing the low level detection at parts per billion levels of structurally unrelated nitrosamines in malt beverages. The objection offered no evidence that the formation of nitrosamines in malt beverages has any possible relevance to structurally dissimilar nitrosamine formation in soft drinks containing aspartame. Nor did the objection present any evidence to rebut the data submitted by the petitioner that these compounds cannot be readily formed in aspartame. The agency therefore concludes that no hearing is required because the objection did not provide any evidence to refute the previous safety determination on nitrosamine formation. Thus, the objection states an allegation, but raises no issue of fact on which to base a hearing.

b. *Toxicity of DKP.* An additional issue raised by the objection was that FDA had "mischaracterized" the results from Lederer's study on DKP and that the agency had "failed to consider adequately the concern" for fetal toxicity (Turner, p. 10). The teratology and reproduction studies conducted by the petitioner in support of its petition for dry uses of aspartame rebut that position (Ref. 25). Moreover, the agency notes that Dr. Lederer acknowledged, prior to the publication of the carbonated beverage rule, that "the conclusions of my work are concordant with those of the U.S.A." (Ref. 26; see also the discussion at 48 FR 31376 at 31380). Consequently, the agency also finds that the objections raise no material issue of fact with regard to potential embryotoxicity, but make an unsupported allegation. FDA will not hold a hearing based on a mere allegation.

D. Consumption Levels

Mr. Turner's objection alleges that in concluding that aspartame was safe for carbonated beverage use, the agency improperly estimated consumption levels of aspartame because (1) FDA failed to include additional individuals likely to consume carbonated beverages; (2) FDA based consumption levels on understated or nonexistent calculations; (3) the use patterns on consumption in the petition were not correct; (4) FDA did not consider the consumption of products containing aspartame at the three main meals; (5) FDA did not include consumption of aspartame in hot weather in the estimate; (6) FDA used the "gross national population consumption formula" to calculate consumption; (7) intake greater than the previous acceptable daily intake is unsafe (Turner, pp. 19–23).

Various consumption estimates, including estimates of aspartame exposure resulting from the consumption of carbonated beverages containing aspartame, were exhaustively considered by the Board's decision at p. 14 to p. 22 and by the Commissioner in his final decision approving aspartame for dry uses (46 FR 38285 at 38289–38290). Mr. Turner argued in the earlier proceeding that the consumption levels were underestimated and the Board and the Commissioner considered but rejected these arguments. Thus, Mr. Turner has been given a full opportunity to present his views on consumption.

FDA believes further that the objection demonstrates a basic misunderstanding of how the agency

calculates the estimated daily intake (EDI) of food additives, and how these dietary exposure estimates relate to the acceptable daily intake (ADI) of the additive. The agency is therefore discussing the important principles used to develop consumption estimates.

The EDI is a measure of chronic dietary exposure of the additive from all food sources in which it is used; it is the day-in and day-out estimated intake over a particular span of an individual's lifetime. The ADI is the amount of a compound that can be safely consumed each day on a chronic basis; it is derived primarily from chronic toxicological studies in animals. Levels of consumption may occasionally rise above or fall below the EDI. Daily carbonated beverage consumption, for example, may be greater in hot weather. The important safety issue is whether the EDI exceeds the ADI. Both of these figures may change as chronic consumption patterns change. The EDI will increase as the use of the additive is extended to other food categories, and the ADI may be revised as more toxicological information is evaluated. For example, prior to the approval of the use of aspartame in carbonated beverages, the agency increased the ADI from 20 to 50 mg/kg body weight, because additional toxicological data from clinical studies submitted by the petitioner demonstrated that the new level was safe (Ref. 10).

The allegations that FDA failed to include additional individuals likely to consume carbonated beverages, that carbonated beverage consumption was understated or that consumption calculations do not exist are simply untrue. Searle and FDA calculated the maximum EDI of aspartame during the proceedings leading to the approval of aspartame for dry use and again during the evaluation of the carbonated beverage petition using three different methods. FDA reviewed each of these estimates (46 FR 38285 at 38289; 48 FR 31376 at 31377). Each of the EDI exposure estimates, including the 34 mg/kg body weight estimate ultimately accepted by the Commissioner (46 FR 38285 at 38290), explicitly included aspartame intake from carbonated beverages or was even broader in scope. (See 46 FR 38289–38290 for a complete discussion of consumption levels.) One estimate assumed that aspartame replaced all sucrose in the diet of an average male, and another assumed that aspartame replaced all carbohydrate in that diet.

The objection alleges that the patterns of consumption in the petition were not correct but submitted no data to show that actual use patterns differ from those calculated by Searle and FDA. FDA calculates dietary exposure estimates of new direct food additives by applying data on food consumption, as established by surveys, and data on the concentration of the additive in foods. The data submitted by Searle dealt with all aspects of aspartame consumption including consumption with other foods, such as the three main meals. In its petition for carbonated beverage approval, Searle included a new calculation that relied on the most recent survey data compiled by the Market Research Corp. of America (MRCA). MRCA survey data are compiled from dietary records kept throughout the year by 4,000 U.S. households. Estimates using MRCA data are based on the foods actually eaten by people in various age brackets and include data from both average and heavy users in particular food categories. Prior to approving aspartame for use in carbonated beverages, the agency reviewed the Searle calculation and computed its own values for aspartame exposure from all foods (Ref. 27). The agency's evaluation specifically recorded the percentage increases in estimated aspartame exposure resulting from carbonated drink consumption, and concurred with the petitioner's method of calculation, but restated the exposure estimate to reflect "eaters only." This estimate of EDI is based on those people who actually consume the product and maximizes EDI figures for any particular age group, because it does not average in the nonconsumer in the survey population.

On an occasional day, for example in hot weather, intake levels of aspartame may exceed the ADI. However, this occasional excess would not result in chronic intake above the ADI. Whether it is safe to ingest levels of a substance on some days in excess of the established ADI depends on how acutely toxic the additive is. Clinical tests of aspartame at doses of 200 mg/kg body weight, which exceeds the ADI, were performed and submitted by Searle in support of its petition (Ref. 6). In these studies, the acute effect of the ingestion of single doses of 200 mg/kg of aspartame on blood levels of amino acids and methanol were found to be well below toxicological levels of concern (48 FR 31376 at 31381). Thus, Mr. Turner's observation that the consumption of six cans of beverage containing aspartame on a hot day will result in exposure that exceeds the ADI is not a credible basis for alleging that the agency has "understated" consumption levels (Turner, p. 21). The consumption by a 20 kg child of six 12-ounce cans of orange beverage sweetened with aspartame would result in an exposure of 100 mg/kg of aspartame, which is well below the 200 mg/kg dose administered in Searle's clinical study without any sign of acute toxicity (Ref. 6) and even further below the levels of toxicological concern. (Six 12-ounce cans of orange beverage sweetened with aspartame (.93 mg per milliliter) would contain approximately 2,008 mg of aspartame.) Accordingly, the objection fails to present credible evidence raising a material issue of fact. The objection is also based on a demonstrably false premise.

As discussed above, the agency has estimated that the highest likely chronic consumption of aspartame per day would be 34 mg/kg body weight. The objection contended that aspartame consumption will not always occur in a "throughout the day" pattern, but would occur principally in large doses, that is, at meals when individuals are most likely to consume food and aspartame-containing beverages at the same time (Turner, p. 20). The agency does not regard the possible consumption of aspartame in a single large dose as posing any safety problem whatsoever. During the evaluation of the petition for the dry uses of aspartame, the agency analyzed the toxicity from acute exposure to aspartame. FDA relied upon a study in which high single doses of up to 200 mg of aspartame per kg of body weight were given to human subjects (Ref. 6). With respect to acute toxicity, the pattern of aspartame ingestion over the day is not important as long as the total amount ingested per day does not exceed the 200 mg/kg level shown to be safe.

Finally, FDA is not familiar with the term "gross national population consumption formula" mentioned in the objection and is unable to determine its relevance to the issue of aspartame consumption (Turner, p. 22). Presumably, the objection is suggesting that FDA should adopt an entirely new policy regarding estimates for food additive consumption instead of its current policy, which is described above and is used in estimating the projected consumption of food additives. The current policy and possible alternatives to it are not at issue in this proceeding, nor are they proper issues for a formal evidentiary public hearing. Moreover, the objection presents no evidence describing this proposed new consumption formula, or establishing its validity.

FDA is denying the request for a hearing on the consumption issue for a

number of reasons. First, Mr. Turner was a party to the earlier proceeding in which consumption estimates were an important issue. He raised essentially the same consumption issue there. The Board's decision at p. 14 to p. 22 and the Commissioner's decision (46 FR 38285 at 38307) each discussed the matter and ruled against Mr. Turner's objection. Mr. Turner could have sought judicial or administrative review of the earlier decision. He did not do so. He cannot now complain, because he has had a full and fair opportunity to present his views and be heard. Moreover, his objections present no data in support of his position.

E. Carcinogenicity Potential of Aspartame and its Metabolites

1. *Aspartame's potential for causing brain tumors.* Mr. Turner objects to the approval of aspartame for use in carbonated beverages because "the Commissioner and the agency have not adequately dealt with the recommendation of the Public Board of Inquiry that approval of aspartame be withheld pending results from further oncogenic studies with the additive" (Turner, p. 15). Interpretation of the results of the chronic rat feeding studies designed to determine aspartame's potential for causing brain tumors was one of the major scientific issues before the Board, and consequently one of the most comprehensively deliberated issues bearing on aspartame's safety. The Board found that the results of these tests were not sufficiently conclusive and recommended that approval of aspartame be withheld pending results from further oncogenic studies with the additive (Board's decision at p. 49). The Commissioner disagreed with the Board's findings and concluded that there was a reasonable certainty that aspartame does not cause brain tumors in rats (46 FR 38285 at 38295). Mr. Turner was a party to that earlier proceeding and made the same objection to the regulation approving dry uses of aspartame. He recieved a formal hearing on that objection. Mr. Turner now contends that the Board's findings, rather than the Commissioner's findings, were correct. Mr. Turner's current objection did not, however, submit any new data on this issue.

In his final decision (46 FR 38285 at 38295), the Commissioner explained why he disagreed with the Board's findings that more studies were needed on the carcinogenic potential of aspartame. This decision is supported by the record which included not only the three chronic studies before the Board but also negative results observed in a subsequent animal study not available to the Board (Ref. 28).

The administrative record shows that the approval of aspartame in supported by a complete series of toxicological tests in animals. These studies have been thoroughly reviewed by FDA scientists. Based on that review and for the reasons stated in the Commissioner's decision, the agency reaffirms the conclusion that there is a reasonable certainty that aspartame does not cause brain tumors in rats.

Mr. Turner had a fair opportunity to present his arguments and have them fully considered in the proceeding leading to the approval of aspartame for dry uses. He had an opportunity to challenge the Commissioner's decision in the Court of Appeals. He chose not to do so, and is thus estopped from relitigating the issue in the absence of new evidence. He has presented no new evidence in support of his position here, and thus has raised no material issue of fact that justifies a further hearing in this proceeding.

2. *Uterine polyps in rats.* Mr. Turner's objection states that "* * * neither the Commissioner nor the agency has recognized 'precancerous polyps' in the approval of aspartame for use in carbonated beverages" (Turner, p. 34). The polyps in question originated in the uteri of rats chronically administered the diketopiperazine-derivative of aspartame (DKP) for 2 years (Ref. 29). The study data in question were submitted to the agency in support of Searle's original food additive petition for aspartame. Subsequently, as a result of FDA's concern over the issue, the agency referred the raw data to four independent teams of pathologists at FDA, the Massachusetts Institute of Technology, the Armed Forces Institute of Pathology, and G.D. Searle for review. Prior to convening the Board, those teams identified cystic endometrial hyperplasia, which is commonly referred to as uterine polyps, as the most common lesion. Cystic endometrial hyperplasia occurs in aging rats spontaneously and is most commonly associated with age-related endocrine disturbances. Uterine polyps are considered to be a localized form of endometrial hyperplasia and have no tendency to undergo malignant transformation and, therefore, are not considered precancerous in nature (Ref. 30).

The Searle study also supports a safety factor of about 1,000 with respect to the induction of uterine polyps. Thus, the agency concludes that the possibility that uterine polyps will occur as the result of aspartame ingestion is very remote (Ref. 29).

Because the polyps were not considered precarcinogenic, they were not an issue specifically addressed by the Board and the Commissioner. Nonetheless, Mr. Turner could have raised the issue at the hearing or before the Commissioner. He could have sought judicial review of the Commissioner's decision, but did not. He has had an adequate opportunity to be heard.

3. *Carcinogenic potential of formaldehyde.* The objections stated that there are no studies available for FDA to use in assessing the chronic toxicity and carcinogenic potential of methanol and formaldehyde formed from methanol metabolism in the body (Monte, p. 4; Turner, p. 12).

The agency does not agree with this assertion. In its original submission to FDA in support of the use of aspartame for dry uses, Searle included the results of chronic feeding studies of aspartame in the dog, the mouse, and the rat (Ref. 31). The results of another chronic study that corroborate the Searle study are available through the open literature (Ref. 28). One of the major objectives of this type of chronic study is a comprehensive histopathological examination of virtually all organ systems in order to assess both the chronic toxic and carcinogenic potential of the administered compounds.

Before approving the original petition for aspartame for dry uses, FDA analyzed the chronic feeding studies and concluded that aspartame was safe. Although these studies were designed to assess the toxicity and potential carcinogenicity of aspartame, they also tested the toxicity and potential carcinogenicity of aspartame's metabolites. The metabolic studies submitted by the petitioner demonstrate that all ingested aspartame is broken down in the gastrointestinal tract into its constituents, aspartic acid, phenylalanine, and methanol. Because the aspartame molecule is 10 percent methanol by weight and because the dosages used in the chronic studies were quite high (rat: 1 to 8 g/kg body weight, mouse: 1 to 4 g/kg body weight, and dog: 1 to 4 g/kg body weight), the exposure of these species to methanol in these four chronic studies was as high as 400 to 800 mg/kg body weight per day, a very significant dose. Based on an ADI for human exposure of 50 mg of aspartame per kg body weight per day (or 5 mg/kg body weight of methanol), these doses represent an 80- to 160-fold exaggeration of methanol exposure in the chronic animal studies when compared with the very high but

conceivable levels of human exposure to methanol through aspartame ingestion.

The Searle studies also ensured comparable dosages and durations of exposure to formaldehyde, because, as discussed above, methanol is metabolized to formaldehyde on a one-to-one molar basis. Thus, contrary to the objections, both methanol and formaldehyde were thoroughly tested, and FDA reviewed the results of those tests prior to approving aspartame for dry uses.

The hearing request cites a recent study indicating that formaldehyde, administered intranasally to rats, produced carcinomas at the site of application—the nasal turbinates (Ref. 32). The site of the carcinomas strongly indicates that the neoplastic process is a localized, not a systemic, reaction to the known irritating and cytotoxic properties of formaldehyde. No increase in tumor incidence was observed at sites remote to direct exposure (Ref. 32). The same study supports the further conclusion that direct exposure to relatively high concentrations of formaldehyde gas is necessary before the carcinogenic process occurs.

In addition, there is another series of chronic studies in the scientific literature, which FDA considered prior to the approval of aspartame for dry uses, in which hexamethylenetetramine was administered in the drinking water in doses of 0.5 to 5 percent to three strains of mice for 60 weeks and to Wistar rats in drinking water at 1 percent for 104 weeks (Ref. 33). Because hexamethylenetetramine is broken down in the acid medium (Ref. 34) of the stomach to formaldehyde, these studies directly tested whether orally administered formaldehyde is carcinogenic (Ref. 33). In the hexamethylenetetramine studies, no evidence of carcinogenic activity was found in any of the test groups.

The fact that aspartame when ingested in doses up to 8 gm/kg body weight (800 mg/kg formaldehyde) produced no carcinogenic effect is strong evidence that formaldehyde exposure from the oral route of administration is without carcinogenic risk. Any question regarding adequacy of dosing from these studies is resolved by the results from the studies with hexamethylenetetramine where doses of up to 1,500 mg/kg body weight formaldehyde were ingested by mice and rats without any carcinogenic effect. Thus, the inhalation study is not appropriate for use in determining whether formaldehyde is a systemic carcinogen and in evaluating the safety of aspartame. There is no issue of fact, because it has been demonstrated that formaldehyde is not a systemic carcinogen. No hearing is required, because the objection does not submit sufficient evidence to raise a serious question about aspartame's systemic carcinogenicity. Although the agency does not believe that a hearing is justified in view of the hexamethylenetetramine studies, the objectors may request reconsideration as provided in 21 CFR 10.33 and are free to submit comments on the hexamethylenetetramine studies, or on any other studies that are or may become available.

4. *Two human cancers in clinical studies.* One of the objections claims that the Commissioner failed to assign sufficient significance in his decision approving aspartame for dry uses to the finding of two human cancers at the eleventh week of a 13-week study on aspartame (Turner, p. 17). One insulin-dependent diabetic developed an adenocarcinoma of the breast and one non-insulin-dependent diabetic developed a reticulosarcoma of the stomach.

The agency as well as a reviewing pathologist concluded that these types of cancer are associated with a pathological process requiring many months to years for development into a malignant phase. Therefore, the cancers arising in these two patients receiving aspartame were considered to be coincidental and unrelated to aspartame intake.

As with so many of Mr. Turner's objections, that issue was before the Board and the Commissioner in the earlier proceeding. Mr. Turner could have appealed the Commissioner's decision. That he chose not to do so means that he may not raise the issue again at this time. He has had an adequate opportunity to be heard, and no new hearing is required.

F. Interpretation of Data From Clinical Studies

Mr. Turner's objection alleges that FDA failed to give adequate credence to the potential for adverse reactions related to the use of aspartame observed in the clinical studies (Ref. 35). The objection pointed out that there were five times as many complaints reported by aspartame users as by the control group in that study (Turner, p. 22).

FDA did evaluate these results. The clinical study referred to in the objection was only one of several clinical studies, which included normal adults and children, as well as obese and diabetic adults, conducted by the petitioner and submitted to the agency in support of its petition on dry uses of aspartame (Ref. 7). Based on an analysis of the results from all these studies, FDA concluded that there was no evidence of any consistent or obvious pattern of specific complaints from aspartame use.

All the data from these studies were available prior to the earlier hearings. Mr. Turner could have raised the issue at the hearing or before the Commissioner but did not do so. He has had an adequate opportunity to be heard, and no hearing is required on the issue. Moreover, in the absence of any additional data bearing on the clinical study, Mr. Turner's objection constitutes nothing more than an allegation, and raises no material issue of fact upon which a hearing could he held.

G. Quality of Data

One objection claims that the research submitted by G. D. Searle should not have been relied upon for evaluating the safety of aspartame because the research was conducted in a flawed and inaccurate manner (Turner, p. 23). This issue was presented to the Commissioner in the earlier proceeding on the dry uses of aspartame and although decided adversely to Mr. Turner, he failed to seek judicial or administrative review of the issue. Although Mr. Turner is estopped from relitigating this issue a second time, the agency has nevertheless considered it and concluded that the quality of the data is adequate.

The agency believes that there has been an adequate confirmation of the quality of the studies to provide reliable evidence for the safety assessment of aspartame. In fact, a comprehensive review of the authenticity of the aspartame research data was performed on the 15 pivotal studies submitted by G. D. Searle. Three of these studies were audited by FDA and 12 by UAREP. This was a massive undertaking and took over 2 years to complete. UAREP concluded that the studies were authentic and, on December 13, 1978, submitted to FDA its 1,062 page report. The agency agreed with UAREP that those 12 studies, as well as the 3 studies which it had reviewed, were indeed authentic. In addition to determining the authenticity of these studies, the report by UAREP also contained detailed observations of how these studies were conducted.

Although UAREP, like the agency, noted some procedures and irregularities that warranted improvement, none were of such a serious nature as to invalidate an entire study. In view of the fact that the objection has provided no new information on the quality or design of Searle's data, the agency believes that it

is adequately addressed in the Commissioner's final decision on aspartame (46 FR 38285 at 38301).

H. Labeling of Food Containing Aspartame

One objection contends that foods containing aspartame are not adequately labeled, but provides no information to support the position that current requirements are insufficient (Monte, p. 10). Current regulations require that the label of any food containing aspartame shall bear a prominent and conspicuous notice to phenylketonurics that the product contains phenylalanine.

No other susceptible consumer group has been identified by the objection, nor has it identified the "substantial dangers" (Monte, p. 10) posed by the regulated uses of aspartame. Accordingly, the agency concludes that the issue raised is one of policy, not fact, and is not resolvable by a hearing.

V. Summary and Conclusions

Under 21 CFR 170.3(i), the safety of a food additive means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. FDA's regulations reflect the Congressional judgment that the additive must be properly tested and the tests carefully evaluated, but the additive need not, indeed cannot, be shown to be safe to an absolute certainty. As the House of Representatives Report on the Food Additives Amendment stated:

Safety requires proof of a reasonable certainty that no harm will result from the proposed use of the additive. It does not—and cannot—require proof beyond any possible doubt that no harm will result under any conceivable circumstance.

H.R. Report No. 2284, 85th Cong., 2d Sess., 1958.

Aspartame has been exhaustively tested for safety and the data have been reviewed by the agency over the course of 11 years. In addition, FDA referred portions of the safety on aspartame to outside groups of scientists for additional review, prior to approving aspartame for dry uses. The safety testing conducted for aspartame surpasses the testing requirements for direct food additives developed by the agency and set forth in its "REDBOOK" (Ref. 4). As discussed in Section I. above, the safety issues associated with the dry uses of aspartame were the subject of additional scrutiny at a hearing before the Public Board of Inquiry conducted by three scientists. Finally, the Commissioner reviewed the safety issues and the Board's conclusions on them so that he could reach a final decision on the safety of aspartame for dry uses.

After reviewing all the points raised in the objections, FDA concludes that the following issues were fully dealt with in the earlier proceeding leading to the approval of aspartame for dry uses: brain lesions and mental retardation, consumption levels, aspartame's potential for causing brain tumors, uterine polyps in rats, two human cancers and other alleged adverse reactions in clinical studies, and the quality of Searle's safety data submitted in support of the dry uses of aspartame. In the current proceeding, Mr. Turner submitted an objection covering each of these points even though, as had been pointed out before, he was a participant in the earlier proceeding. He had the opportunity to present evidence before the Board of Inquiry; he had the opportunity to question participants in that hearing; and he had the opportunity to and did file exceptions to the Board's findings. He also had the opportunity to appeal the Commissioner's decision on the dry use petition to the Court of Appeals as provided by section 409(g)(1) of the act (21 U.S.C. 348(g)(1)) or to petition for administrative reconsideration under 21 CFR 10.33. He has thus had a full and fair opportunity to present his case and have it considered in the proceeding on the dry uses of aspartame. No more is required.

The objections in the current proceeding have raised some points that present issues of law and policy, not issues of fact, specifically the allegations concerning safety testing requirements for decomposition products, consumption estimates, and labeling requirements. As explained in the specific sections discussing these points, FDA will not hold a hearing where the objection raises only issues of law or policy because these kinds of issues are not proper for resolution at a hearing.

One objection argued that because formaldehyde produced tumors at the site of administration (intranasally) in rats, FDA could not properly conclude that this metabolite of aspartame was not a systemic carcinogen. The objection offered no additional data, other than the reference to the intranasal study, that could be relied upon to solve the issue at a hearing. Considered in its factual setting, this study is inadequate to justify a conclusion that formaldehyde is a systemic carcinogen. FDA will not grant a hearing if the material submitted, even if accurate, is insufficient to justify the factual determinations urged.

Finally, the objections made a number of unsubstantiated allegations, specifically that aspartame might cause potential adverse behavioral effects, that various decomposition products of aspartame may be toxic, that the consumption estimates of aspartame are inaccurate, and that aspartame may cause cancer. In each of these cases, the objections have proferred no data on which a meaningful hearing might be based. Thus, no hearing is required on those issues.

For the reasons stated in this conclusion and in the discussion above, FDA is denying the objections and requests for a hearing.

Dated: February 17, 1984.

Mark Novitch,

Acting Commissioner of Food and Drugs.

Appendix—References

The following information has been placed on display in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, and may be reviewed in that office between 9 a.m. and 4 p.m., Monday through Friday.

1. Letter from R. J. Wurtman to Sanford A. Miller, July 21, 1983.

2. Wurtman, R. J. letter to the editor, *New England Journal of Medicine*, 309:429-430.

3. Letter from P. A. LaChance to Anthony Brunetti, December 2, 1982.

4. Food and Drug Administration, "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food," **Federal Register** of October 15, 1982 (47 FR 46141).

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8. Food Additive Master File 134, Studies E-37, E-38, E-42, E-48, E-56, and E-57.

9. Food Additive Master File 134, Studies E-50, E-68, and E-71.

10. FAP 2A3661, Memoranda from Food Additives Evaluation Branch, January 18 and March 15, 1983.

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